

Docket N .: Schaller  
Serial N .: 09/383,978

**CLEAN VERSION OF AMENDED CLAIMS**

- Sub E1
1. (Twice amended) A method for expressing a heterologous gene in hepatocytes in culture comprising:
- providing replication defective hepadnavirus particles at a titer level competent to infect hepatocytes, wherein the region of the S-gene of the hepadnavirus genome has been replaced with the heterologous gene of up to 800 basepairs, such that the expression of the heterologous gene is regulated by the regulatory sequences of the S-gene;
  - infecting hepatocytes with the hepadnavirus such that the heterologous gene is delivered into the hepatocytes and expressed in the hepatocytes, and wherein the replication defective hepadnavirus particles are one of human hepatitis B virus or duck hepatitis B virus particles
4. (Twice amended) The method of claim 42, wherein the heterologous gene replaces the S-gene under control of an endogenous S-promoter.
33. (Thrice amended) A replication defective hepadnavirus particle of the group consisting of human hepatitis B virus and duck hepatitis B virus, wherein a region of an S-gene of the hepadnavirus genome has been deleted and replaced by a heterologous gene such that the sequences that are essential for reverse transcription are retained.

Docket No.: Schaller  
Serial No.: 09/383,978

39. (Thrice amended) A method of producing replication defective hepadnavirus particles of human hepatitis B virus and duck hepatitis B virus at a titer suitable for infecting hepatocytes in culture comprising:

- DE  
E
- co-transfecting hepatocyte cells of a hepatoma cell line with:
    - (i) replication defective hepadnavirus constructs, wherein a region of an S-gene of the hepadnavirus DNA has been replaced with a gene encoding a heterologous gene, such that expression of the gene encoding a cytokine is regulated by regulatory sequences of the S-gene; and
    - (ii) a helper construct for transcomplementing lacking viral gene products;
  - culturing the hepatocytes until infectious viral particles are produced; and
  - recovering the infectious particles.

42. (Twice amended) A method for producing replication defective recombinant hepadnavirus particles capable of expressing a heterologous gene in hepatocytes in culture comprising:

- DE  
E
- replacing an S-gene in a hepatitis B virus genome with the heterologous gene of up to 800 base pairs such that the expression of the heterologous gene is regulated by an S-promoter;

Docket No.: Schaller  
Serial No.: 09/383,978

- producing a replication deficient hepadnavirus by means of a helper plasmid transcomplementing viral gene products such that the lacking viral gene products are present;
- Infecting hepatocytes with the recombinant hepadnavirus in culture, whereby the heterologous gene is delivered into the hepatocyte and expressed in the hepatocyte, wherein the replication defective recombinant hepadnavirus particles are human hepatitis B virus particles.

*DB*  
*Case 2*

43. (Twice amended) A recombinant hepatitis B virus genome, wherein an S-gene in the genome is deleted and replaced by a heterologous gene of up to 800 base pairs and wherein the genome is selected from the group consisting of recombinant human hepatitis B virus or recombinant duck hepatitis B virus, and wherein the sequences essential for reverse transcription are retained.
-